Specification (see e.g. pages 10-13). No new matter has been added by any of these amendments.

Response to Rejections

35 U.S.C. § 112, second paragraph

Claims 8-14, 16-28, and 30-35 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Without necessarily agreeing with the propriety of the rejection, claims 8-14 and 21-35 have been canceled thereby obviating this rejection. Applicants have submitted new claims 36-59 to replace these claims. The new claims more clearly set forth the claimed invention. In addition, Applicants note that claim 16 has been amended herein for technical clarity and to more clearly set forth the claimed invention.

In light of the cancellation of the claims and claim amendments submitted herein, Applicants submit that the claims now clearly define the invention. Applicants respectfully request the Examiner to withdraw the rejection.

35 U.S.C. § 102, Brenner *et al.*

Claims 8-14, 21, 23-28, 30-33 and 35 were rejected under 35 U.S.C. § 102(e) as being anticipated by Brenner *et al.*, U.S. Patent No. 5,863,722 (hereinafter "Brenner"). Basically the Examiner suggests that Brenner anticipates these claims because Brenner discloses the preparation of microparticles or beads with polynucleotides attached thereto. The Examiner further notes that solid phase supports that are used include beads, or microspheres. The practice of employing microparticles with polynucleotides or nucleic acids thereon is described, wherein enzymatic processes are observed. Finally, the Examiner asserts that Brenner discloses the utilization of bioactive agents for decoding ligands to complementary tags. Applicants traverse the rejection and note that the rejection is moot because the rejected claims have been cancelled. However, Applicants will address Brenner in light of the new claims, with an emphasis on the independent claims.

As the Examiner is aware, "[i]t is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367 (Fed. Cir. 1986). As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference." See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1497 (Fed.Cir 1995).

New claim 36 is drawn to a method for decoding an array composition comprising providing an array comprising substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein the sites are wells, and a population of microspheres randomly distributed on the sites, wherein the population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label. The method further includes decoding a location of the bioactive agent by correlating the bioactive agent with the location. New claims 52, 54 and 58 similarly include the limitation that the array includes a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein the sites are wells and beads are distributed on the sites.

Brenner, however, fails to disclose that beads are distributed in wells on a substrate wherein the wells (discrete sites) are at a density of at least 100 sites per 1 mm^2. Accordingly, Brenner fails to anticipate claims 36, 52, 54, 58 and those claims that depend from them.

New claim 52 is directed to a method for decoding an array composition comprising providing an array comprising substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2 wherein the sites are wells and a population of microspheres randomly distributed on the sites, wherein the population comprises at least a first and a second subpopulation each comprising a different bioactive agent and a different identifier binding ligand and decoding a location of the bioactive agent by correlating the bioactive agent with the location. Likewise, claim 58 includes the limitation that the microspheres of each subpopulation each include a different bioactive agent and a different identifier binding ligand.

However, Brenner fails to teach that the microspheres each contain a different bioactive agent and a different identifier binding ligand. That is, the Examiner suggests that Brenner teaches bioactive agents as wells as identifier/decoder ligands because in addition to tags on beads, Brenner teaches the "utilization of identifier binding ligands, such as biotin...with avidin attachment/decoding entities on the solid support". However, initially Applicants note that in this context biotin/avidin are used to immobilize the microspheres, not to "decode" them. In addition, Applicants note that because only biotin/avidin is disclosed, each subpopulation of microspheres cannot have a different identifier ligand. As such, Brenner fails to anticipate claims 52, 58 and those that depend from these claims.

Accordingly, Brenner fails to teach each and every element of the presently pending claims. Therefore, Brenner does not anticipate the present invention; Applicants respectfully request the Examiner to withdraw the rejection.

35 U.S.C. § 102, Chelsky *et al.*

Claims 8-14, 16, 17, 21, 23-25, 30, 31, 33, and 35 were rejected under 35 U.S.C. § 102(e) as being anticipated by Chelsky *et al.*, U.S. Patent No. 5,856,083 (hereinafter "Chelsky"). Basically the Examiner asserts that Chelsky anticipates these claims because Chelsky discloses a lawn assay wherein solid supports such as beads are randomly immobilized on a lawn at discrete sites such as the bottom of a petri plate followed by the application of test enzyme, which test enzyme decodes the beads regarding the presence or absence of enzyme activity therewith. Applicants respectfully traverse the rejection. In addition, as to the rejection of claim 8-14, 21, 23-25, 30, 31, 33, and 35, Applicants note that the rejection is moot following cancellation of these claims. However, Applicants will address Chelsky as it relates to claim 16 and the new claims.

Claim 16 is directed to a method of making a microsphere array comprising contacting a substrate with a surface comprising discrete sites, at a density of at least 100 sites per 1 mm^2, with a solution comprising a population of different particles, wherein the particles do not comprise an optical signature and applying energy to the substrate or the solution, or both, such that at least a subpopulation of the different particles randomly associate onto sites.

In contrast, there is no teaching in Chelsky of discrete sites at a density of at least 100 sites per 1 mm^2. Accordingly, Applicants submit that Chelsky fails to teach each and every element of the claim 16.

In addition, as to the newly submitted claims, Applicants note that all of the claims included the limitation that the discrete sites (or wells) are at a density of at least 100 sites per 1 mm^2. Thus, Chelsky does note anticipate the claims on this basis.

Therefore, Chelsky does not anticipate every element of the present invention, and Applicant respectfully requests withdrawal of the rejection.

Provisional Double-Patenting Rejection

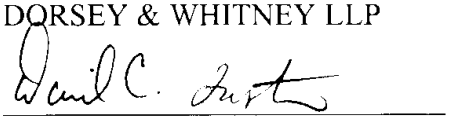
Claims 8-14, 16-28, and 30-35 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 15-22, and 24 of copending application Serial No. 09/748,706.

Most of the rejections are moot in light of the cancellation of the claims herein. However, with respect to claims 16-20 and as the rejection may be applied to the newly submitted claims, Applicants note that since this is a provisional double patenting rejection, the Examiner is requested to resolve the remaining issues and give an indication of otherwise allowable subject matter with regard to one of the pending cases per the guidance provided in M.P.E.P. §§ 804 and 822.01.

CONCLUSION

Applicant submits that the claims are in condition for allowance and early notification to this effect is solicited. The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues remain.

Respectfully submitted,
DORSEY & WHITNEY LLP



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AppendixB: Version to Show Changes Made

16. (Twice Amended) A method of making a microsphere array comprising:

a) contacting a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, with a solution comprising a population of different particles, wherein said particles do not comprise an optical signature; and

b) applying energy to said substrate or said solution, or both, such that at least a subpopulation of said different particles randomly associate onto sites.

The following claims are new:

- -36. (New) A method for decoding an array composition comprising:

a) providing an array comprising:

i) substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said sites are wells; and

ii) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label; and

c) decoding a location of said bioactive agent by correlating said bioactive agent with said location.

37. (New) The method according to claim 36, wherein said bioactive agents are nucleic acids.

38. (New) The method according to claim 37, wherein said nucleic acids are DNA.

39. (New) The method according to claim 37, wherein said nucleic acids are single stranded nucleic acids.

40. (New) The method according to claim 37, wherein said nucleic acids are double stranded nucleic acids.

41. (New) The method according to claim 36, wherein said bioactive agents are proteins.

42. (New) The method according to claim 36, wherein said substrate is a fiber optic bundle.

43. (New) The method according to claim 36, wherein said substrate is glass.

44. (New) The method according to claim 36, wherein said substrate is plastic.

45. (New) The method according to claim 36, 37, 38, 39, 40, 41, 41, 43 or 44, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

46. (New) The method according to claim 45, wherein said first and second decoder binding ligand comprise first and second different labels.

47. (New) The method according to claim 36, 37, 38 or 38, whereby said decoding comprises contacting said array with at least a first and second different nucleic acid decoder binding ligand, whereby said first and second different nucleic acid decoder binding ligand hybridizes with said first and second bioactive agents, respectively, to thereby identify a location of said frist and second bioactive agents to thereby decode said array.

48. (New) The method according to claim 36, 37, 38, 39, 40, 41, 42, 43 or 44, wherein each subpopulation further comprises a different identifier binding ligand.

49. (New) The method according to claim 48, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligand, whereby said first and second identifier binding ligand identifies said first and second bioactive agent, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

50. (New) The method according to claim 49, wherein said first and second decoder binding ligands comprise first and second labels.

51. (New) The method according to claim 49, whereby said first and second different identifier binding ligands are different nucleic acids and said first and second decoder binding ligands are nucleic acids that hybridize to said first and second identifier binding ligands, respectively.

52. (New) A method for decoding an array composition comprising:

a) providing an array comprising:

i) substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said sites are wells; and

ii) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising:

a. a different bioactive agent; and

b. a different identifier binding ligand; and

b) decoding a location of said bioactive agent by correlating said bioactive agent with said location.

53. (New) The method according to claim 52, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to said first and second identifier binding ligand, whereby said first and second identifier binding ligand identifies said first and second bioactive agent, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

54. (New) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with an array comprising:

i) substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said sites are wells; and

ii) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label;

b) determining the presence or absence of said target analyte; and

c) decoding a location of said bioactive agent by correlating said bioactive agent with said location.

55. (New) The method according to claim 54, wherein said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

56. (New) The method according to claim 54, wherein each subpopulation further comprises a different identifier binding ligand.

57. (New) The method according to claim 56, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligand, whereby said first and second identifier binding ligand identifies said first and second bioactive agent, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

58. (New) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with an array comprising:

i) substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said sites are wells; and

ii) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising:

a. a different bioactive agent; and

b. a different identifier binding ligand;

b) determining the presence or absence of said target analyte; and

c) decoding a location of said bioactive agent by correlating said bioactive agent with said location.

59. (New) The method according to claim 60, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligand, whereby said first and second identifier binding ligand identifies said first and second bioactive agent, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.- -.